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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,899	01/06/2006	Christine Beswick	010180.00031	6636

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,899	BESWICK ET AL.	
	Examiner	Art Unit	
	EMILY BERNHARDT	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22-24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,22-24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of II in the reply filed on 4/15/08 is acknowledged. The claims will only be examined with respect to the elected invention, which is limited to "A" ring of formula IIA that is heterocyclic. Thus X and Y as CH is not within the elected scope.

Claims 1-20,22-24 and 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Nature of optional substituents permitted throughout the variables is not clearly defined in the specification. While a list of intended moieties are described on p.9-10 , the intended scope is not limited to said list. Note the wording "for example". A similar issue was present in Ex parte Remark 15 USPQ 2d 1498 (at p.1500) in which it was decided that claim language that relied on open-ended language was "vague and uncertain" since it was not clear what else was intended to be covered. The rejection can be overcome by making the definition close-ended in the specification .

2. In claim 17 "optional substituent" is recited for "R" which is not clearly defining intended scope. Also while this claim is dependent on 1, it does not say if "Q" is as defined in claim 1 as recited for many other variables.

3. Method claim 22 is of indeterminate scope for more than one reason.

Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. Additionally, determining whether a given disease responds or not to "inhibition of HSP90 activity" involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? Further exacerbating the scope is the fact that such proteins are involved in chaperoning a number of client proteins and thus may affect directly or indirectly all normal cell functions. The test for determining compliance with 35 USC 112, par.two is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

4. In claim 22 "in particular" is not clearly defining the invention as its not clear what is being claimed- subject matter before or after the term.

5. Is claim 23 a compound or a composition claim? If the former it is not further limiting claim 1's scope since intended uses in compound claims are

given no material weight. Note In re Tuominen 213 USPQ 89. If the latter is intended a carrier should be recited consistent with its pharmaceutical application. Note that claim 24 dependent on 23 fails to further limit the scope of 23 . See Tuominen which is on point.

Claims 1-20,22-24 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for remaining recited forms, does not reasonably provide enablement for solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Solvates are nonenabled since generally not all solvents can form solvates with all compounds. There is no process enabling such a scope in the specification . Note Vippagunta provided in herein who flatly states on p.18, section 3.4 the following: "Predicting the formation of solvates or hydrates of a compound.... Is complex and difficult." Applicants' own specification confirms this since despite numerous examples presented none of the final products were obtained as solvates. Pursuant to In re Wands, 8 USPQ2d 1400, factors such as 1) direction or guidance- none is seen in the specification as to what solvent would be suitable except for water; 2) presence or absence of

working examples- there is none in the present case; 3) breadth of the claims- scope is easily in the millions; and 4) quantity of experimentation needed to make or use the invention must be considered to determine if undue experimentation is present. With regard to quantity of experimentation needed, it would be enormous given compounds of the instant scope would need to be synthesized and then exhaustively crystallized from the gamut of solvents reported to form solvates in the literature, followed by an examination of the crystal structure to see if any solvate has formed.

Claims 1-20,22-24,26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Scope of elected substituted pyrazoles being claimed is not remotely enabled. An assortment of rings can be present as substituents at Ar as well as at Cyc and Q which can be both mono- and poly-fused which in turn can be even further substituted. Assay testing for 98 compounds is reported in the specification but these are not representative of the elected

claims' scope given that the majority of compounds have H at R1/R2. Ar is always phenyl with substitution thereon representative of the scope in 5,6 or 7. For "A" mainly piperazines have been tested and to a lesser degree piperidines and morpholines with the type of substituents embraced in claims 13 and 14. However, there is no reasonable assurance as to what other rings/chains at these various locations will work as there is no actual test data reported but only an upper or lower range labelled as "A" or "B" and in view of the lack of any absolute data reported, there is no insight into structure-activity trends that need to be evaluated. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the billions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature involving inhibitory activity of a particular protein (HSP90) of the class known as "heat shock protein". HSP90 is known to interact with at least 300 proteins (such as Akt) having a variety of regulatory functions. Other proteins form complexes with HSP90 to assist the HSP90 protein in maintaining stability and viability of cells undergoing some form of stress response. Research in this area is very preliminary as only recently has evidence been discovered showing how the regulatory proteins associated with cancer seem to interact with HSP90.

It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18. Note recently published Barril (2006), which evidences structure-sensitivity for instant compounds at various positions;

3) Direction or guidance- as stated above the compounds actually made and tested represent a small fraction of what is claimed;

4) State of the prior art- The compounds are pyrazole derivatives with the requirement that at the 3-position the rings must be aromatic and at the 4-position non-aromatic. Such compounds are described as being

HSP90 inhibitors. No such compounds of similar structure have been described in the prior art for any activity much less the one relied on herein;

5) Working examples- While test data has been presented it is directed to a very homogeneous class of compounds and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

Claims 22,26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. No evidence is presented that instant compounds have such a myriad of uses including treating any cancer, virus or inflammatory disease or remaining uses being claimed. Note Dymock publication (available online as indicated on PTO-892; electronic copy would not import into current file) emphasizes how preliminary the findings are regarding the biological process relied on herein in the field of cancer treatment. See

concluding remarks therein on p.844. Compounds having entered Phase I clinical trials such as 17AAG are not reported to be broad-based anti-tumor agents much less useful to treat any and all viral, inflammatory diseases . No evidence of clinical progress for such uses is seen in the reported literature. Note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Level of unpredictability in the art- The invention is pharmaceutical in nature involving a complex mechanism which is not much understood as discussed in the references above;

2) Direction or guidance- The amount of guidance presented in the specification as to which compounds are sufficiently active to be useful for the claimed uses is nonexistent . The dosage range information (on p.15) is virtually useless being a 30,000 - fold range and not directed to a specific disease;

3) Working examples- While test data has been presented only assay testing has been reported with no absolute data and thus it is by no means clear how active these compounds actually are. Thus in the absence of animal studies and in the absence of any correlation between studies

conducted **in vitro** and the diseases to be treated, there is no sufficient evidence to support the claimed uses.

In view of the above considerations, this rejection is being applied.

Applicants' IDS filed 5/27/05 cannot be considered at this time as none of the references are seen in the electronic file. Copies are thus requested for consideration.

Applicants may wish to request a corrected filing receipt as there is an error in the foreign priority date. Note the year is in error.

A search in the pertinent art area for the elected invention showed nothing teaching or suggesting the mandatory features required herein, notably at "A". US'534 is made of record as it has similar features but lacks a clear teaching of elected "A" rings claimed herein. DE'329 is directed to identical compounds nut is not a competent reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-

272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Bernhardt/
Primary Examiner, Art Unit 1624

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